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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,367	08/22/2001	Michael Wigler	TUIN.002.05US	1838
1473	7590	10/06/2004	EXAMINER	
FISH & NEAVE LLP 1251 AVENUE OF THE AMERICAS 50TH FLOOR NEW YORK, NY 10020-1105			KIM, YOUNG J	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/935,367

**Applicant(s)**

WIGLER ET AL.

**Examiner**

Young J. Kim

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 19-31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/6/2002</u> . | 6) <input type="checkbox"/> Other: ____.  |

## **DETAILED ACTION**

### ***Preliminary Remark***

The preliminary amendment received on August 22, 2001, canceling claims 1-18 and adding claims 19-31 is acknowledged.

Applicants are advised that the previously submitted CRF had errors and the notice to comply had been mailed out on January 21, 2004. Applicants are requested to review their record to see if the new CRF had been submitted.

### ***Priority***

Applicants are advised that Applicants' petition to claim priority to parent application 09/261,079, filed on March 2, 1999, the issued U.S. Patent therefrom, said patent number, 6,277,606, issued on August 21, 2001, has been dismissed on February 2, 2004.

As the filing date of the instant application is after the issuance of the patent on the above-recited parent application, the priority claim is not valid, and therefore, the priority claim under 35 U.S.C. 120 is denied.

Therefore, the effective filing date of the instant application is the actual filing date of the application, the filing date being August 22, 2001.

### ***Drawings***

The drawings received on August 22, 2001 are acceptable.

### ***Specification***

For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate

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paragraph unless it appears in an application data sheet. ***The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression “now Patent No. \_\_\_\_\_” should follow the filing date of the parent application.*** If a parent application has become abandoned, the expression “now abandoned” should follow the filing date of the parent application.

It appears that the most current the status of the parent applications are not recited.

Appropriate correction is required.

### ***Information Disclosure Statement***

The IDS received on March 6, 2002 is acknowledged. A signed copy of its PTO-1449 is attached hereto.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 27, 29, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the following reasons. Claim 1 recites the phrase, “carrying out a first round of the following steps for enrichment of target DNA: removing said first set of adaptors from ***said amplicons*** and ligating a second set of adaptors to the 5’ ends of the amplicons of tester DNA,” but the term, “said amplicons” include both the driver amplicons and the tester amplicons. When claims are read in light of the specification, it appears that the

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adaptors are **not** removed from the driver amplicons nor second adaptors ligated to the driver amplicons, wherein on page 7, lines 15-25 of the specification recites, “the tester amplicon fragments (after the removal of the first adaptors and attachment of the second adaptors), **are then combined with the driver amplicon fragments and melted and allowed to reanneal.**”

Claims 1, 29, and 31 are indefinite for reciting the phrase, “substantially completely digesting separately the DNA,” because the term, “substantially” is contradicted by the term, “completely,” because term, substantially denotes the meaning, “partially,” and therefore, it is unclear how a DNA molecule can be digested completely and partially at the same time.

Claim 27 is indefinite for reciting the phrase, “identifying sites that differ between two different related eukaryotic DNA sources,” because it is unclear what is meant by the phrase, “identifying sites,” means identifying sequence differences, identifying different regions along the DNA. For the purpose of prosecution, the phrase is assumed to mean identifying sequence differences between two different related eukaryotic DNA sources.

Claim 31 recite the limitation, “said cancer cell and said normal cell.” There is insufficient antecedent basis for said limitation. For the purpose of prosecution, claim 31 is assumed to depend from claim 29, which contains the antecedent basis for the above-recited limitation.

Applicants are advised to amend the claims identifying the line and page number of the specification from which support could be found. Generic statement stating that the support for the amendment are “replete throughout specification,” would jeopardize a possible new matter rejection.

***Claim Rejections - 35 USC § 102***

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 20, and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Fischer (U.S. Patent No. 5,876,932, issued March 2, 1999).

Claim 19 is drawn to a DNA probe from a first eukaryotic DNA, wherein the method of producing said probe results in a restricted DNA molecule with adaptors ligated thereto.

Fischer discloses a cDNA probe comprising a ligated adaptor at its end(s) (Figure 1), thereby anticipating instant claim 19. The product by which the claimed probe is produced has no patentable weight so long as the characteristic of the final product is met by the product of the prior art. As already discussed, the DNA probe produced by the recited method of claim 19 is a restricted DNA fragment comprising a ligated adaptor at its end. Since Fischer discloses such a DNA probe, claims 19, 20, and 24 are anticipated. Additionally, the practice of the method of Fischer would necessarily generate a pool of such DNA probes, thereby anticipating claim 28.

Fischer discloses that the resulting DNA could be excised from the electrophoretic gel, reamplified, and cloned for further analysis (column 1, lines 47-19), as well as a kit comprising the reagents of the method (column 12, lines 25-26), thereby anticipating claims 25 and 26.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 19-28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al. (U.S. Patent No. 5,565,340, issued October 15, 1996, filed January 25, 1995) in view of Malek et al. (U.S. Patent No. 5,712,127, issued January 27, 1998, filed April 29, 1996).

Chenchik et al. disclose a method of exponentially amplifying a target-specific "tester" DNA involving the use of a driver DNA, wherein said method can be used for identifying differences between tester and driver genomic sequences, said method comprising the steps:

(a) ligation of dephosphorylated adaptors to the tester DNAs and the driver DNAs, wherein said tester DNA comprises a different adaptor than that of the driver DNAs;

(b) combining under melting and annealing conditions, said tester DNA with excess of driver DNAs, whereby a portion of the resulting double stranded DNA comprises self-annealed tester DNA;

(c) amplifying the tester DNA via use of primers, resulting in their exponential amplification (Figure 4; column 14, lines 18-37).

While Chenchik et al. performs all of the steps recited in the enrichment step recited by instant claim 19, Chenchik et al. do not employ the steps of fragmenting the tester DNA and the driver DNA, followed by the ligation of the first adaptors followed by their amplification, prior to their enrichment step.

Malek et al. disclose a well-known method of reducing complexities of DNAs, wherein dephosphorylated adaptors are ligated to tester and driver DNAs that are generated with a frequently cutting restriction endonucleases, wherein the ligated DNAs are separately amplified,

followed by their cleavage with the same restriction endonuclease to remove the adopter sequences (column 3, lines 9-22).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Chenchik et al. by addition of a preceding method step, said method step being well-known method of reducing complexities of DNA samples of Malek et al. for the following reasons.

The method of Chenchik et al. allows exponential amplification of the desired target nucleic DNA via use of driver DNAs which comprise different adopter sequences. The same configuration is employed by the “enrichment” step of the instant claims. Whether or not such enrichment step is preceded by a step of reducing the complexity of sample DNA, is determined in view of the statement by Malek et al. who demonstrates a technique well-established and known in the art for reducing complexities of sample DNAs, such as RDA, which reduces the complexities of the tester and driver DNAs (column 3, line 20-22; column 2, lines 30-44), to generate fragments of particular length that can be efficiently amplified in PCR as “representations” of the genome (column 2, lines 34-35).

Therefore, one of ordinary skill in the art would have been easily motivated to first reduce the complexity of a genomic DNA by a well-known method such as RDA, followed the method of Chenchik et al. which allows exponential amplification of the target DNA and therefore, efficient detection of the target DNA sequence.

MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success. As Malek et al. state that RDA can be followed by an amplification method, one of ordinary skill in the art at the time the



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invention was made would have had a reasonable expectation of success at combining the method of Chenchik et al. which is also an amplification method.

With regard to the probes limitation, Chenchik et al. disclose that their method can be employed to discover, "new probes for pathogenic organisms" (column 14, lines 34-35), or in a method of identifying inherited disorders (column 14, line 37), thereby meeting the limitation of claims 19-28 and 31.

With regard to the limitation wherein the excess of driver DNA being at least about 5-fold of the tester DNA, determination of optimal conditions which require routine experimentation is considered to be well within the purview of an ordinarily skilled artisan.

With regard to the method of Chenchik et al. being used for cancer detection, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the teaching for detection of sequence differences correlated with hereditary diseases, as suggested by Chenchik et al. (at column 14, line 37), such as cancer detection.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer (U.S. Patent No. 5,876,932, issued March 2, 1999).

While Fischer is not explicit in that the claimed probe is derived from a genomic DNA, viral DNA, or pathogen DNA, Fischer discloses that due to its sensitivity, the method can be used to isolate new genes (genomic DNA), identify new gene family of interest, define different life stages of an organism, examine life cycle of a cell and how it deviates from the normal cycle, etc.

Based on the suggestion of such wide applicability, it would have been obvious to one of ordinary skill in the art at the time the invention was made, to apply the teachings of Fischer for detections of organisms such as pathogens and virus, for the advantage of detection sensitivity of the target nucleic acids, wherein the practice of such method would necessarily produce the probes of the instant claims.

Therefore, the invention as claimed is obvious over Fischer.

### ***Conclusion***

No claims are allowed.

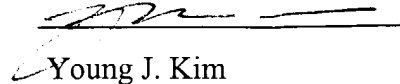
### ***Inquiries***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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Young J. Kim  
Patent Examiner  
Art Unit 1637  
9/30/04

**YOUNG J. KIM**  
**PATENT EXAMINER**

yjk